Case Presentation

Common cutaneous signs unmasking a severe hematological disorder: GATA2 deficiency

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Abstract

GATA2 deficiency is a rare genetic disorder with heterogeneous clinical manifestations affecting the immune, hematologic, and vascular systems. We report the case of a 31-year-old woman with primary lymphedema progressing since childhood, associated with diffuse treatment-resistant warts and severe monocytopenia. Genetic testing revealed a mutation in the *GATA2* gene (c.1078T>C), resulting in complete loss of protein function. The patient also exhibited leukopenia and anemia, and bone marrow evaluation confirmed progression to acute myeloid leukemia. The immune deficiencies caused by this mutation explain the increased susceptibility to recurrent infections, particularly persistent human papillomavirus infections responsible for the extensive warts in this patient. The frequent progression to myelodysplastic syndromes and leukemia underscores the severity of this condition and the importance of early diagnosis. Management requires close monitoring, with hematopoietic stem cell transplantation representing the only curative option to improve prognosis and prevent progression to life-threatening complications. This case highlights the need for prompt identification of GATA2 mutations in patients with suggestive clinical features to optimize surveillance and treatment.

Introduction

The *GATA2* gene, located on the long arm of human chromosome 3 at cytoband 3q21.3, encodes a transcription factor involved in hematopoiesis, angiogenesis, and lymphatic vessel development.[1] Pathogenic mutations in *GATA2* result in variable clinical manifestations, including myelodysplastic syndrome, acute leukemia, immune deficiencies with a high frequency of viral, bacterial, or fungal infections, pulmonary findings such as alveolar proteinosis, vascular manifestations such as lymphedema, and hearing loss. The median age at onset is approximately 20 years, although some individuals remain clinically asymptomatic. The 10-year survival rate from symptom onset is estimated at 84%.[2]

To date, roughly 500 patients with GATA2 deficiency have been reported, with inheritance confirmed as autosomal dominant in 50% of cases, de novo in 5%, and uncertain in the remainder.[3] We describe a case of GATA2 deficiency in a 31-year-old woman presenting with primary lymphedema, profuse warts, and monocytopenia.

Case Synopsis

We report the case of a 31-year-old woman presenting with primary lymphedema of the lower limbs, progressively worsening since the age of 8 years. The patient reported recurrent respiratory infections during childhood without a definitive diagnosis and had no significant family history. She presented to our dermatology department for diffuse warts resistant to conventional treatments. Clinical examination revealed lymphedema of the lower limbs, more pronounced on the right side (**Figure 1**), associated with multiple warts of varying sizes with a rough, hyperkeratotic surface. In some areas, the lesions coalesced into thick, irregular plaques on the lower limbs (**Figure 2**), with extension to the upper limbs (**Figure 3**), as well as flat warts on the face.

Initial laboratory studies showed severe monocytopenia at 0 × 10^9/L (reference: 0.1–0.6 × 10^9/L) and leukopenia at 2 × 10^9/L (reference: 4–10 × 10^9/L), along with normochromic, normocytic, non-regenerative anemia at 9 g/dL. Given this constellation of findings, GATA2 deficiency was suspected and subsequently confirmed by genetic

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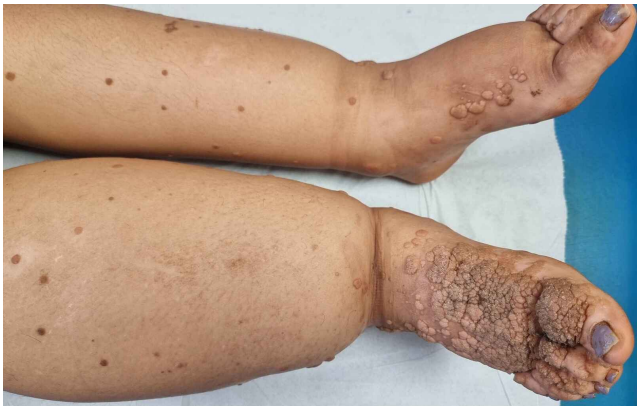

Figure 1. *Bilateral lymphedema of the lower limbs, more pronounced on the right side.*

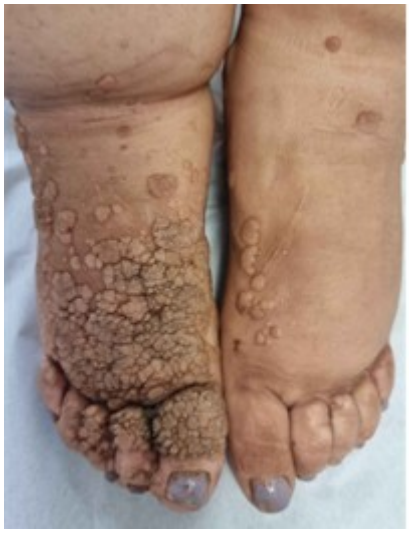

Figure 2. *Multiple keratotic verrucous lesions on the anterior surfaces of the feet.*

analysis. DNA extraction was performed using the Qiagen DNA extraction kit (Qiagen, Hilden, Germany), followed by molecular analysis via a 40-gene sequencing panel that included the *GATA2* gene. Sequencing identified a missense variant, NM_032638.5:c.1078T>C (p.(Trp360Arg)), located at nucleotide position c.1078 in exon 5. This heterozygous substitution (T to C) results in the replacement of tryptophan with arginine at position 360 of the protein sequence. Advanced modeling of the protein structure and biophysical properties using 3-dimensional missense analysis indicated that this variant is likely to cause structural damage and disrupt GATA2 protein function.

Bone marrow aspiration confirmed progression to acute myeloid leukemia, revealing a predominance of blasts (**Figure 4**). A thoracic computed tomography scan showed no abnormalities. A genetic study of both parents is planned to evaluate potential hereditary transmission.

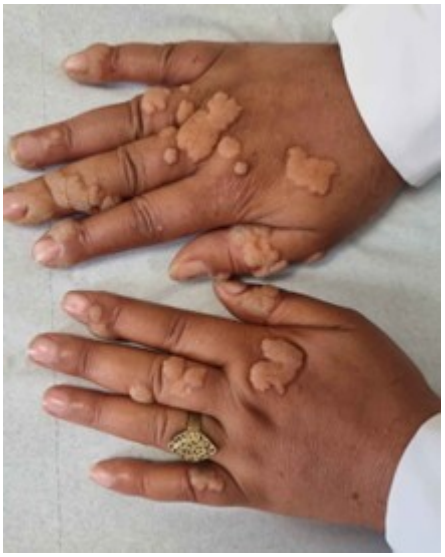

Figure 3. *Multiple warts on the posterior surfaces of the hands.*

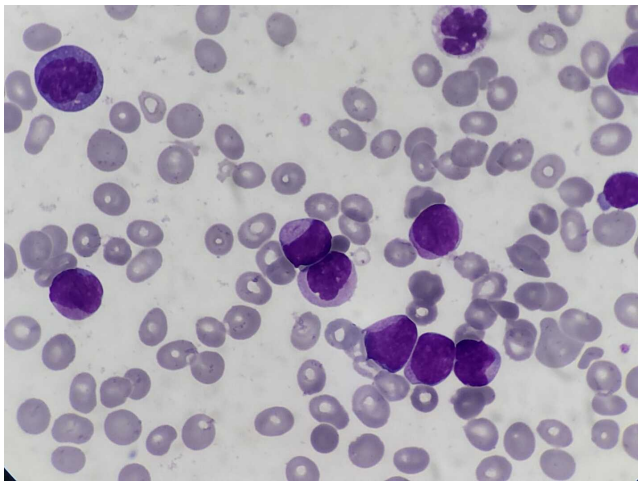

Figure 4. *Microscopic analysis of the bone marrow demonstrating marked dysplasia with an excessive number of blasts, consistent with bone marrow dyscrasia (May-Grünwald-Giemsa, original magnification × 1000).*

Case Discussion

The clinical manifestations of GATA2 deficiency result from the loss of multilineage progenitor cells, leading to cytopenias affecting B lymphocytes, monocytes, natural killer cells, and dendritic cells. These immunological alterations predispose patients to recurrent and severe infections, including viral infections in approximately 70% of cases—most commonly caused by human papillomavirus (HPV)—as well as severe bacterial infections (49%) and fungal infections (16%). Marked monocytopenia is specifically associated with a high susceptibility to non-tuberculous mycobacteria, reported in 53% of patients.[2] This vulnerability is linked to disruption of the IFNγ–IL12 axis, which plays a critical role in host defense against intracellular pathogens.[4] These immunological

deficiencies explain the characteristic presentation of refractory, recurrent warts and chronic pulmonary infections. In our patient, the profuse HPV-related warts illustrate this typical defect in antiviral immunity.

From a hematological perspective, bone marrow failure initially presents as hypocellularity with dysmegakaryopoiesis, commonly progressing to myelodysplastic syndrome or acute myeloid leukemia. In some cases, myeloid malignancy may even constitute the first clinical manifestation, occurring in the absence of other typical features.[5] A study of French and Belgian patients with GATA2 deficiency estimated the risk of evolving to myelodysplastic syndrome or acute myeloid leukemia at 39% by age 20 years, increasing to 80% by age 40 years.[6] Bone marrow biopsies often show hypocellular marrow for age, and cytogenetic abnormalities—such as monosomy 7, trisomy 8, and somatic mutations in genes including *ASXL1* and *STAG2*—are critical for progression toward malignancy.[7,8] In the present case, evolution to leukemia further confirms the high leukemic risk associated with GATA2 deficiency.

Extracellular manifestations, though less frequent, also contribute significantly to the clinical picture. Lymphedema, present in 11% of cases, typically begins in childhood or adolescence and most often affects the lower limbs and genitalia, reflecting the essential role of GATA2 in lymphatic vessel development. Additional manifestations include sensorineural hearing loss (76%), pulmonary alveolar proteinosis (18%), and ventilation disorders (63%). Recurrent miscarriages, reported in 33% of affected women, further illustrate the multisystemic impact of this condition.[6]

Management requires a multidisciplinary approach integrating preventive strategies, close monitoring, and curative treatment when indicated. Hematopoietic stem cell transplantation remains the only therapeutic intervention capable of restoring normal hematopoiesis and preventing progression to severe complications such as life-threatening infections and malignant transformation. Indications for transplantation include severe or recurrent infections, progressive cytopenias, myeloid progression with cytogenetic abnormalities or somatic mutations, and pulmonary alveolar proteinosis.[9] The best outcomes are achieved when transplantation is performed early—prior to progression to myeloid malignancy—with reported 4-year overall survival rates as high as 85%.[10] Post-transplant mortality is primarily driven by severe infections and graft-versus-host disease, emphasizing the need for individualized conditioning regimens.

When transplantation is not immediately feasible, management focuses on preventive measures such as HPV vaccination, prophylaxis against environmental mycobacteria, and regular immunological assessments. Close surveillance of asymptomatic or minimally symptomatic patients is critical for detecting early signs of progression toward myelodysplastic syndrome or acute leukemia. Emerging biomarkers such as FLT3-ligand, although still used experimentally, may hold promise for monitoring disease evolution and guiding treatment decisions.[11,12]

Conclusion

This case underscores the importance of maintaining a high index of clinical suspicion when encountering seemingly common manifestations such as diffuse warts and primary lymphedema, as these may reveal severe underlying hematologic disorders, including acute myeloid leukemia. The identification of a *GATA2* gene mutation confirms the crucial role of early genetic evaluation in patients presenting with such suggestive features. Optimal management requires a multidisciplinary approach integrating immunological monitoring and timely hematopoietic stem cell transplantation, which remains the only curative option. Early recognition and intervention are essential to improving prognosis and preventing the irreversible complications associated with GATA2 deficiency.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Hsu AP, Sampaio EP, Khan J, et al. Mutations in GATA2 are associated with the autosomal dominant and sporadic monocytopenia and mycobacterial infection (MonoMAC) syndrome. *Blood*. 2011;118:2653-2655. PMID:21670465

2. Spinner MA, Sanchez LA, Hsu AP, et al. GATA2 deficiency: a protean disorder of hematopoiesis, lymphatics, and immunity. *Blood*. 2014;123:809-821. doi:10.1182/blood-2013-07-515528. PMID:24227816

3. Santiago M, Liquori A, Such E, Zúñiga Á, Cervera J. The Clinical Spectrum, Diagnosis, and Management of GATA2 Deficiency. *Cancers (Basel)*. 2023;15:1590. doi:10.3390/cancers15051590. PMID:36900380

4. Wu UI, Holland SM. Host susceptibility to non-tuberculous mycobacterial infections. *Lancet Infect Dis*. 2015;15:968-980. doi:10.1016/S1473-3099(15)00089-4. PMID:26049967

5. Calvo KR, Hickstein DD. The spectrum of GATA2 deficiency syndrome. *Blood*. 2023;141:1524-1532. doi:10.1182/blood.2022017764. PMID:36455197

6. Donadieu J, Lamant M, Fieschi C, et al. Natural history of GATA2 deficiency in a survey of 79 French and Belgian patients. *Haematologica*. 2018;103:1278-1287. doi:10.3324/haematol.2017.181909. PMID:29724903

7. Hsu AP, McReynolds LJ, Holland SM. GATA2 deficiency. *Curr Opin Allergy Clin Immunol*. 2015;15:104-109. doi:10.1097/ACI.0000000000000126. PMID:25397911

8. Wlodarski MW, Collin M, Horwitz MS. GATA2 deficiency and related myeloid neoplasms. *Semin Hematol*. 2017;54:81-86. doi:10.1053/j.seminhematol.2017.05.002. PMID:28637621

9. Belohlavkova P, Hrochova K, Fatorova I, Zak P. MonoMAC syndrome with GATA2 novel mutation: A case report. *Leuk Res Rep*. 2022;18:100346. doi:10.1016/j.lrr.2022.100346. PMID:36119727

10. Nichols-Vinueza DX, Parta M, Shah NN, et al. Donor source and post-transplantation cyclophosphamide influence outcome in allogeneic stem cell transplantation for GATA2 deficiency. *Br J Haematol*. 2022;196:169-178. doi:10.1111/bjh.17840. PMID:34580862

11. Dickinson RE, Milne P, Jardine L, et al. The evolution of cellular deficiency in GATA2 mutation. *Blood*. 2014;123:863-874. doi:10.1182/blood-2013-07-517151. PMID:24345756

12. Bigley V, Haniffa M, Doulatov S, et al. The human syndrome of dendritic cell, monocyte, B and NK lymphoid deficiency. *J Exp Med*. 2011;208:227-234. doi:10.1084/jem.20101459. PMID:21242295